

# Renal protection in off pump coronary artery bypass grafting

Citation for published version (APA):

Kanchi, M. (2020). *Renal protection in off pump coronary artery bypass grafting*. [Doctoral Thesis, Maastricht University]. Maastricht University. <https://doi.org/10.26481/dis.20201110km>

## Document status and date:

Published: 01/01/2020

## DOI:

[10.26481/dis.20201110km](https://doi.org/10.26481/dis.20201110km)

## Document Version:

Publisher's PDF, also known as Version of record

## Please check the document version of this publication:

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## Valorization

The present thesis introduces and studies the frequency and causes of renal damage in cardiac surgery patients, with an emphasis on off pump coronary artery bypass grafting. Which is especially important for a country like India where as many as 90% of CABG is being done as an off-pump procedure.

The incidence of renal damage associated with CABG surgery is rather high, and there is evidence that the rate of this complication increased during the last decade. About 2.3% of isolated CABG cases is vulnerable to AKI, and the incidence is higher (14%–15%) in patients with preoperative chronic kidney disease.<sup>1</sup> It has been shown that even a small increase in serum creatinine in the postoperative period, is an independent risk factor for increased mortality.<sup>2-5</sup> Not surprisingly the occurrence of renal dysfunction adds to the length of ICU stay, hospital stay and the cost of treatment.<sup>6-8</sup>

Better understanding of the etiology of renal complications and the development of methods how to prevent them will pave the way for better outcome in CABG surgery. Cardiopulmonary bypass (CPB) and consequent changes in homeostasis are recognized as a main risk factor contributing to the development of AKI in cardiac surgical patients. Hemodilution, emboli either particulate, or gaseous, or micro, or macroscopic, as well as intraoperative haemodynamic instability and all causes of postoperative low output syndrome, all may be involved in the genesis of AKI in patients undergoing cardiac surgery.<sup>9-11</sup>

Renal function is better preserved in patients undergoing off-pump CABG than on-pump CABG. According to our data (Chapter 2) avoiding CPB leads to the more than 50% decrease in renal dysfunction in early postoperative period. Increased age proves to be a risk factor for patients undergoing on-pump CABG and hence elderly people have to be preferably allocated to off-pump rather than to on-pump CABG.

However, the causes which determine the occurrence of renal complications following CABG are not limited to the deleterious effects of CPB only. Among the important preoperative factors are advanced age, reduced left ventricular function, and emergency surgery, preoperative use of intraaortic balloon pump, elevated preoperative serum glucose and creatinine.<sup>9,12</sup> Multivariate logistic analysis (Chapter 3), demonstrated that, in addition to the complexity of surgery, the following factors independently predicted acute renal injury requiring renal replacement therapy ( $p < 0.05$ ): preoperative critical state, pre-existing renal dysfunction, preoperative diastolic dysfunction, and combined cardiac surgery. The genetic predisposition for the development of renal injury after the surgery has been addressed also. Previous genome wide association studies (GWAS) done in Caucasians have identified up to 9 genetic polymorphisms in CABG patients developing AKI.<sup>13</sup> Evaluation of genetic polymorphism of Indian population uncovered 18 genes associated with the development postoperative AKI (Chapter 4). Further investigation in this area could result in discriminating specific pathophysiological mechanisms of renal injury and a more exact definition of the group of patients requiring special attention in renal protection during surgery.

The pharmacological renal protection during cardiac surgery is one of the most discussed topics in literature. In the past decades, many drugs such as dopamine agonists, sodium bicarbonate, *N*-acetylcysteine, antioxidants and atrial natriuretic peptide (to name but a few) were investigated for a possible nephroprotective action in both surgical and ICU patients, however, never with great results.<sup>14-16</sup> In particular, no drug has been clearly proven to prevent the progression of AKI towards the need for RRT and, most disappointing, end-stage renal failure and 'chronic' haemodialysis.<sup>17</sup> Unfortunately, our data (Chapter 6) also did not support the hope for the effectiveness of *N*-acetylcysteine in the prevention of renal dysfunction after off-pump coronary artery bypass

surgery. However, infusion of sodium bicarbonate in off-pump coronary artery bypasses grafting in patients with renal dysfunction did reduce the incidence of Stage-1 AKI by about 40% when compared to a placebo group (Chapter 7).

To conclude, most of the questions discussed in this thesis are at the frontline of the quest for safer cardiac surgery, reducing the frequency and severity of renal injury. This thesis demonstrates the necessity in careful selection of patients prone to renal injury by comorbidities, age or even genetic factors. These patients require special attention in preoperative treatment, intraoperative support, and postoperative care. Using our results, we hope to be able to allocate all patients to their designated care modality and decrease the frequency of renal injury during cardiac surgery.

And last, but not least, this thesis provides a clear definition of directions for further investigations in the prevention of AKI in patients undergoing off-pump CABG.